Role of Neuroinflammation in Brain Tumor Progression: Microglia–Astrocyte Crosstalk as a Therapeutic Target

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1 BACKGROUND

Brain tumors, particularly gliomas such as glioblastoma, are highly aggressive cancers with poor prognosis and limited treatment success. Neuroinflammation plays a critical role in shaping the tumor microenvironment and driving disease progression **[1]**. In this context, resident glial cells microglia and astrocytes—undergo tumor-induced phenotypic changes and become actively involved in tumor biology. Instead of acting as passive supporters these cells promote tumor growth, facilitate immune evasion, and contribute to therapy resistance **[2]**. Understanding the crosstalk between glial cells and tumor cells is essential for developing novel and more effective therapeutic strategies.

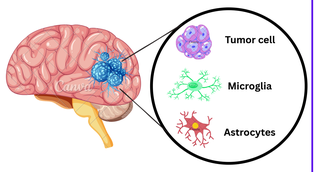

Figure 1: Glioblastoma

2 OBJECTIVE

To investigate how microglia–astrocyte crosstalk drives neuroinflammation in brain tumors and identify potential therapeutic targets within the tumor microenvironment.

8 RESEARCH GAP

1. Current research lacks a detailed understanding of how microglia–astrocyte interactions change across different tumor regions and during treatment.
2. Moreover, no clinically validated, biomarker-guided therapies exist that simultaneously target both glial cell types to effectively disrupt tumor-supportive signaling.

4 ROLE IN TUMOR PROGRESSION

INVASION & MIGRATION	IMMUNE EVASION	ANGIOGENESIS	THERAPY RESISTANCE
MMPs and cytokines degrade ECM to enhance tumor spread	IL-10, TGF-β and PD-L1 suppress anti-tumor immunity	VEGF and hypoxia signaling promote vascular growth	Astrocyte–tumor interactions (Cx43, EVs) reduce response to TMZ and radiation

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3 MECHANISM OF ACTION

MICROGLIA ACTIVATION
Tumor signals
Activate Microglia

CYTOKINE RELEASE
Microglia release
IL-1β, TNF-α.

ASTROCYTE ACTIVATION
Cytokines activate astrocyte
Astrocytes release
IL-10, TGF-β

PRO-TUNOR EFFECT
Reactive astrocyte secrete VEGF and TGF-β, promoting tumor growth, tumor invasion, Immune suppression, and
Therapy resistance

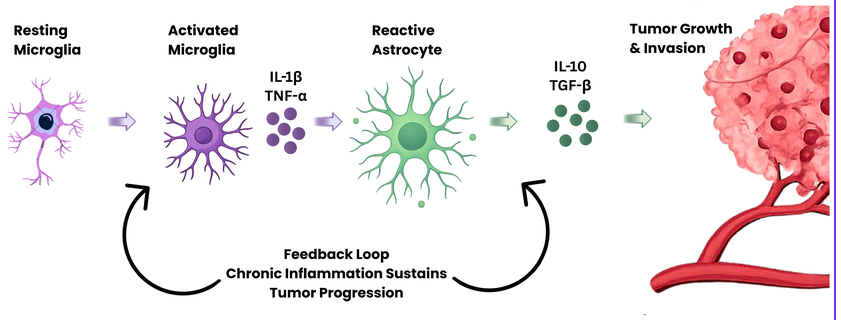


Figure 2: Mechanism of Microglia–Astrocyte Crosstalk in the Brain Tumor Microenvironment

5 CLINICAL RELEVENCE

Residual tumor cells at invasive margins remain protected by the **glial microenvironment.**

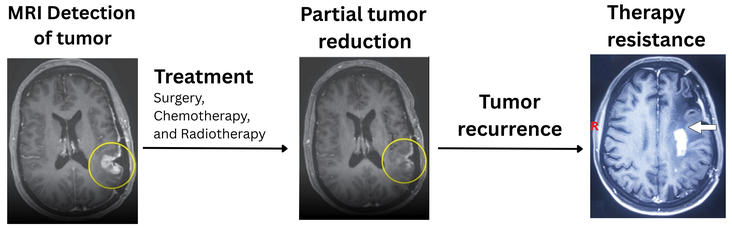
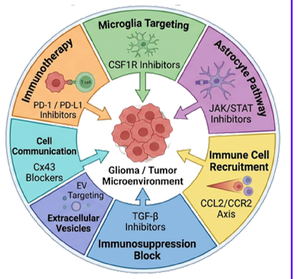


Figure 3 : Tumor Recurrence

6 THERAPEUTIC TARGETS

- **CSF1R inhibitors** that target tumor-associated microglia
- **JAK/STAT pathway inhibitors** that block astrocyte activation
- **CCL2/CCR2** axis that reduce immune cell recruitment
- **TGF-β signaling inhibitors** that limit immunosuppression
- **Cx43 blockers** that disrupt astrocyte–tumor interaction
- **Immune checkpoint inhibitors (PD-1/PD-L1)** that restore immunity
- **Extracellular vesicle targeting** that block communication



7 FUTURE DIRECTIONS

SINGLE-CELL & SPATIAL OMICS	BIOMARKER IDENTIFICATION	DRUG DELIVERY OPTIMIZATION	TARGET DISCOVERY & VALIDATION OPTIMIZATION	COMBINATION THERAPY DEVOLOPMENT	CLINICAL TRANSLATION
Map Glial heterogeneity	Define glial phenotypes	Identify therapeutic pathway	Crossing the BBB	Tumor microenvironment targeting	Validation in clinical trails

9 CONCLUSION

Neuroinflammation plays a central role in brain tumor progression. Microglia–astrocyte crosstalk drives invasion, immune evasion, angiogenesis, and therapy resistance. Targeting this axis offers a promising strategy for precision neuro-oncology. Future therapies should focus on combined tumor + microenvironment targeting.

10 REFERENCES

[1] Bao, Yingshi et al. "From neuroinflammation to gliomagenesis: immune drivers of malignant transformation in the CNS." Frontiers in immunology vol. 16 1682030. 1 Dec. 2025, doi:10.3389/fimmu.2025.1682030.
[2] Xu, Lu et al. "Neuro-immune-tumor axis in gliomas: a review of mechanisms, models, and translational opportunities." Frontiers in immunology vol. 16 1682322. 8 Oct. 2025, doi:10.3389/fimmu.2025.1682322.